

PATENT ABSTRACTS OF JAPAN

(11)Publication number : 2000-229875

(43)Date of publication of application : 22.08.2000

(51)Int.Cl.

A61K 35/78

A61P 3/10

A61P 43/00

C12N 9/99

// A23L 1/30

(21)Application number : 11-030719

(71)Applicant : NIPPON SYNTHETIC
CHEM IND CO LTD:THE

(22)Date of filing : 09.02.1999

(72)Inventor : KAWABATA JUN
KASAI TAKANORI

(54) ALPHA-GLUCOSIDASE INHIBITOR

(57)Abstract:

PROBLEM TO BE SOLVED: To obtain the subject inhibitor having strong α -glucosidase inhibitory activity, being readily taken by making the inhibitor include a plant belonging to the family Compositae as an active ingredient.

SOLUTION: This inhibitor contains a plant belonging to the family Compositae as an active ingredient. For example, chamomile, burdock, Chrysanthemum coronarium, seed of sunflower, etc., may be cited as the plant belonging to the family Compositae and chamomile is preferable. Though the plant belonging to the family Compositae is used in an ordinary state, further dried and powdered or ground in water into a slurried state and the slurried plant may show glucosidase inhibitory activity, an extract obtained by using water and/or an alcohol preferably provides stronger α -glucosidase inhibitory activity. An extract obtained by using a mixed solution of water and an alcohol is especially preferable. Ethanol is preferable as the alcohol. The weight ratio of water/the alcohol is preferably 1/100 to 100/1, more preferably 1/50 to 50/1.

*** NOTICES ***

JPO and NCIP1 are not responsible for any damages caused by the use of this translation.

- 1.This document has been translated by computer. So the translation may not reflect the original precisely.
- 2.**** shows the word which can not be translated.
- 3.In the drawings, any words are not translated.

CLAIMS

[Claim(s)]

[Claim 1] The alpha-glucosidase inhibitor characterized by containing the vegetation belonging to Compositae as an active principle.

[Claim 2] The alpha-glucosidase inhibitor according to claim 1 characterized by making into an active principle the extract which extracted the vegetation belonging to Compositae in water and/or alcohol.

[Claim 3] The alpha-glucosidase inhibitor according to claim 1 or 2 characterized by the vegetation belonging to Compositae being a chamomile.

[Translation done.]

*** NOTICES ***

JPO and NCIP are not responsible for any damages caused by the use of this translation.

1. This document has been translated by computer. So the translation may not reflect the original precisely.
2. **** shows the word which can not be translated.
3. In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the alpha-glucosidase inhibitor which comes to contain the vegetation belonging to Compositae which can be used for drugs, food, health food, a food for specified health use, etc. as an active principle.

[0002]

[Description of the Prior Art] An alpha-glucosidase inhibitor checks the alpha-glucosidase which carries out localization to the microvillus of a small intestine. Controlling the rise of the insulin value following a sudden rise and it of the blood sugar level after a meal In order to be reported to Diabate Medicine, 10, and 688 (1993) and to control the metabolic turnover of carbohydrates (especially the oligosaccharide of the starch origin, sucrose, etc.) also in animals other than human being and human being For example, it is useful to an improvement of various diseases, such as obesity which shows blood sugar rise depressant action and originates in a hyperglycemia symptom and hyperglycemia, and diabetes mellitus. Moreover, the food (health) which added and manufactured the alpha-glucosidase inhibitor fits the diets for patients of a metabolic error, and also fits the still healthier person as metabolic error prevention foods.

[0003] As an alpha-glucosidase inhibitor originating in food, the enzymatic hydrolysis object of an animal protein or vegetable albumen is indicated by JP,9-65836,A, and tea polyphenol is indicated by JP,5-17364,A, for example.

[0004]

[Problem(s) to be Solved by the Invention] However, the alpha-guru KOSHIDA 1 ZE inhibitor given in above-mentioned JP,9-65836,A needed to be too taken in in the large quantity with the tea which must take in in large quantities as food in order to show activity, and purification of polyphenol is complicated and usually takes in with a JP,5-17364,A indication technique. This invention also aims [alpha-guru KOSHIDA 1 ZE inhibition activity] intake strong at offering the easy outstanding alpha-glucosidase inhibitor.

[0005]

[Means for Solving the Problem] Then, as a result of this invention person's inquiring wholeheartedly, the vegetation belonging to Compositae finds out having strong alpha-glucosidase inhibition activity, and came to complete this invention.

[0006]

[Embodiment of the Invention] Below, this invention is stated to a detail.

[0007] Although the seed of a chamomile, a burdock, garland chrysanthemum, and a sunflower etc. is mentioned as vegetation belonging to Compositae of this invention, a chamomile is desirable especially.

[0008] Although what was dried further, disintegration was carried out, or ground [could also use the vegetation belonging to Compositae with the usual gestalt,] it underwater, and was made into the shape of a slurry shows glucosidase inhibition activity, since alpha-glucosidase inhibition activity with the stronger extract in water and/or alcohol is acquired, it is desirable, and the extract in the mixed liquor of water and alcohol is especially desirable. Ethanol is desirable although a methanol, ethanol, propanol, a butanol, etc. are mentioned as this alcohol. What is necessary is just to use the extract approaches, such as a heating extract, continuous extraction, an immersion extract, and supercritical extraction, as an extraction method. When using water and alcohol together, as a mixing ratio (weight ratio) of water/alcohol, 1 / 100 - 100/1 are desirable, and they are 1 / 50 - 50/1 further.

[0009] Specifically, an active principle can be extracted as an extraction method by grinding the vegetation belonging to dry Compositae (drying), being immersed in the water of same weight, and the mixed liquor (the weight ratio of water/alcohol = 1/1) of alcohol, heating this powder, and boiling it for 10 - 30 minutes. Moreover, an active principle can be extracted by dipping this vegetation in the water of same weight, and the mixed liquor (the weight ratio of water/alcohol = 1/1) of alcohol, and heating at neglect or 40-60 degrees C with a room temperature for about 12 to 18 hours for 5 hours - seven days.

[0010] As for above-mentioned water and/or an alcoholic above-mentioned extract, it is desirable to become powder if water and/or alcohol are distilled off, and to use this as an alpha-glucosidase inhibitor. Furthermore, in order to mention effectiveness by little intake, an active principle can be condensed by solvent fractionation actuation in which organic solvents, such as a methanol, ethanol, propanol, a butanol, chloroform, ethyl acetate, toluene, a hexane, and benzene, were used for this extract, and suitable separation purification of an alumina column chromatography, a silica gel column chromatography, gel filtration chromatography, ion exchange chromatography, a canal chromatography, high performance chromatography, etc. can also be further refined by combining one sort or several sorts.

[0011] Since the alpha-glucosidase inhibitor of this invention has blood sugar rise depressant action, it can be diluted with avirulent support, such as solid support, such as liquefied support, such as water, ethanol, ethylene glycol, and a polyethylene glycol, and starch, a cellulose, polyamide powder, and it can be used as drugs, such as the

ampule, a granule, a tablet, a pill, a capsule, and syrups, and health food as a prophylactic of the diets for patients of a metabolic error or a prophylactic, diabetes mellitus, and obesity. Furthermore, the increment in the blood sugar concentration by eating can be controlled by taking the above-mentioned pharmaceutical preparation containing the alpha-glucosidase inhibitor of this invention between after a meal and a meal etc. during time before a meal and a meal.

[0012] As intake of the man at this time, as this (vegetation belonging to Compositae) desiccation powder, a day is desirable in 0.1–50g /, and a day is especially desirable in 0.5–10g /. When using water and/or an alcoholic extract, or the extract stated by the above, the intake of 1 / 1000 – 1/10 of this desiccation powder is sufficient.

[0013] alpha-GURUKO cytase inhibitor of this invention is possible also for adding for food, for example, can also be added in the staple food, a side dish, confectionary, and seasonings, such as solid configuration food, such as liquefied (letter of flow) food, such as coffee, fruit juice, soft drinks, Biel, cow's milk, miso soup, soup, tea, tea, a nutrient, syrup, margarine, and a jam, rice, a pan, a potato product, rice cake, a candy, chocolate, fish flour, a hum a sausage, and a candy As an addition at this time, 0.001 – 85 % of the weight is desirable as desiccation powder of this (it belongs to Compositae) vegetation to the above-mentioned food, and 0.01 – 60 % of the weight is especially desirable. When using water and an alcoholic extract, the addition of 1 / 1000 – 1/10 of this desiccation powder is sufficient. Moreover, the drugs and the health food with which intake was described above also in food, and this appearance are desirable, it is the range which does not check the effectiveness of this invention further, and a sweetening agent, a preservative, a dispersant, a coloring agent, an antioxidant, etc. can be used together. Furthermore, you may use together with alpha-guru KOSHIDA 1 ZE inhibitors which are other well-known alpha-glucosidase inhibitors, such as BARIENAMIN and an amino cyclitol.

[0014]

[Example] This invention is explained concretely below. In addition, it is weight % which is with “%” by the following description.

It filtered, after condensing the immersion fluid which was immersed in the methanol water solution 50 1l.% on the 1st, and was obtained in example 1 chamomile 1kg by the rotary evaporator and dissolving this in water. Vacuum concentration of the obtained filtrate was carried out, and the extract was obtained. This extract was hardened by drying by the rotary evaporator and the solid was obtained. This solid was put into the separating funnel, fractionation of the hexane was carried out to the 30 time weight, in addition the hexane layer (E-1) of solid content, and the water layer, the butanol of weight was added to this water layer 3 times, and the butanol layer (E-2) was extracted. The alpha-glucosidase inhibition activity of each fraction (E-1, E-2) was measured as follows.

[0015] (1) The rat small intestine (jejunum) in which enzyme liquid carried out preparation refrigeration preservation was thawed, and it extracted so that membrane might be extruded with pincettes. It homogenized having added the 0.1M potassium

phosphate buffer solution (pH7.0) which contains 5mM ethylenediaminetetraacetic acid of weight in this membrane 5 times, and cooling. The 0.1M potassium phosphate buffer solution (pH7.0) which contains a triton X-100 1% was added so that centrifugal separation (4 degrees C, 21000xg, 60 minutes) might be carried out after that and it might become weight to the obtained precipitate 5 times, and solubilization processing (4 degrees C, 60 minutes) was performed. Ultra-centrifugal separation (4 degrees C, 110000xg, 90 minutes) of this was carried out, and this supernatant liquid was dialyzed with the 0.01M potassium phosphate buffer solution (pH7.0) (4 degrees C, 24 hours), and it considered as enzyme (alpha-glucosidase) liquid.

[0016] (2) The measurement alpha-GURUKO cytase activity of alpha-glucosidase activity used sucrose as a substrate using the commercial kit. The standard reaction mixture presentation was used as 0.7ml (what dissolved sucrose in the 0.1M potassium phosphate buffer solution pH 6.3) of 60mM substrate solutions, 0.2ml (after carrying out concentration hardening by drying of the part for E-1 obtained from chamomile 0.1g, and E-2-minute formation, it dissolves so that it may be set to 1ml 50% at a dimethyl sulfoxide water solution, respectively) of examined substance solutions, and the 0.1ml (a total of 1.0ml) of the above-mentioned enzyme liquid. This was made to react for 15 minutes 37 degrees C, the reaction was stopped using 1.5ml (pH7.0) of 2M tris hydrochloric-acid buffer solutions, and it considered as test fluid. Next, after adding 50micro of test fluid I to 96 hole microplate per hole at color reagent [glucose B Test Wako (Wako Pure Chem make)] 200microl and incubating for 30 minutes at 37 degrees C, the absorbance of 490nm was measured by the microplate reader (BIO RAD company make, MODEL550). The absorbance when adding the 0.1M potassium phosphate buffer solution (pH6.3) instead of a substrate solution was made into the blank value, and the value which deducted this value was set to A490s. The absorbance when adding a dimethyl sulfoxide water solution 50% of the weight instead of test fluid was made into the control value (A490c), and alpha-glucosidase inhibition activity was searched for by the bottom type.

Measurement was performed twice and the average was made into measured value.

[0017]

[Equation 1] $\alpha\text{-glucosidase inhibition activity (\%)} = [(A490\text{ c} - A490\text{ s}) / A490\text{ c}] \times 100$
 — the alpha-glucosidase inhibition activity of each fraction (E-1, E-2) was shown in Table 1.

[0018]

[Table 1]

分画成分	α -グルコシダーゼ 阻害活性 (%)
E-1	7. 2
E-2	53. 9

[0019]

[Effect of the Invention] Since the glucosidase inhibitor of this invention contains the

vegetation belonging to Compositae as an active principle, it is easy to take in and strong inhibition activity is shown.

[Translation done.]